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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/089,058      | 09/19/2002  | Curtis Braun         | 10447-22            | 2663             |

1059 7590 06/28/2005

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EXAMINER

NAVARRO, ALBERT MARK

ART UNIT PAPER NUMBER

1645

DATE MAILED: 06/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/089,058

Applicant(s)

BRAUN ET AL.

Examiner

Mark Navarro

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-45 is/are pending in the application.
- 4a) Of the above claim(s) 1-12, 22-36, 39-41, 43 and 44 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 13-21, 37, 38, 42 and 45 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 10/30/02.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_.

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election without traverse of Group II, claims 13-21, 37-38, 42 and 45 in the reply filed on April 11, 2005 is acknowledged.

Additionally, the requirement for the election of ricin A and ricin B is withdrawn in view of past practice in Patent Numbers 6,333,303 and 6,531,125. The restriction to a total of 10 elected sequences remains unchanged in view of MPEP 803.04.

Accordingly, claims 1-45 are pending in the instant application, of which claims 1-12, 22-36, 39-41, and 43-44 are withdrawn from further consideration as being drawn to a non-elected invention.

### ***Claim Objections***

1. Claims 21 and 42 are objected to because of the following informalities:

Claims 21 and 42 both exceed the maximum number of sequences that are permitted to be claimed in a single application. Appropriate correction is required.

2. Claim 14 is objected to because of the following informalities: Claim 14 recites the abbreviations "MMP" and "UPA." Abbreviations can often stand for multiple distinct chemicals, for example MMP could represent a tripeptide of methionine-methionine-proline. Amendment of the claims to recite the intended

Art Unit: 1645

molecules in the first instance it appears is suggested. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

3. Claims 13, 15-21, 37-38, and 45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 13, 15-21, 37-38 and 45 recite a recombinant protein having a linker sequence which contains a cleavage recognition site for a “specific protease.”

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a “specific protease” alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The protein itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Art Unit: 1645

*Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed.” The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.”

Applicant is reminded that Vas-Cath make clear that the written description provision of 35 USC 112 is severable from its enablement provision.

Furthermore, in *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that “An adequate written description of a DNA... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention.”

Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 “Written Description” Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

4. Claims 13-21, 37-38, and 45 are rejected under 35 U.S.C. 112, first paragraph, as

Art Unit: 1645

containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 13, 15-21, 37-38 and 45 recite a recombinant protein having an A chain of a "ricin like toxin" and a B chain of a "ricin-like toxin."

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a "ricin-like" alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The protein itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

*Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." The specification does not

Art Unit: 1645

“clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.”

Applicant is reminded that Vas-Cath make clear that the written description provision of 35 USC 112 is severable from its enablement provision.

Furthermore, in *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that “An adequate written description of a DNA... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention.”

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Art Unit: 1645

5. Claims 13-20, and 37-38 are rejected under 35 U.S.C. 102(a) as being anticipated by Borgford.

The claims are directed to a recombinant protein comprising an A chain of a ricin-like toxin and a B chain of a ricin like toxin and a heterologous linker amino acid sequence, linking the A and B chains, wherein the linker sequence contains a cleavage recognition site for a specific protease.

Borgford (WO 98/49311) disclose of a protein having an A chain of a ricin-like toxin, and a B chain of a ricin like toxin and a heterologous linker amino acid sequence linking the A and B chains. Borgford further disclose that the linker sequence contains a cleavage recognition site for a disease specific protease such as a cancer, fungal, viral or parasitic protease. (See abstract and claims).

6. Claims 13, 15-20, and 37-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Borgford.

The claims are directed to a recombinant protein comprising an A chain of a ricin-like toxin and a B chain of a ricin like toxin and a heterologous linker amino acid sequence, linking the A and B chains, wherein the linker sequence contains a cleavage recognition site for a specific protease.

Borgford (WO 97/41233) disclose of a protein having an A chain of a ricin-like toxin, and a B chain of a ricin like toxin and a heterologous linker amino acid sequence linking the A and B chains. Borgford further disclose that the linker sequence contains a cleavage recognition site for a retroviral protease such as HIV or HTLV protease. (See abstract and claims).



***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 13-20, and 37-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borgford in view of Kappler et al.

The claims are directed to a recombinant protein comprising an A chain of a ricin-like toxin and a B chain of a ricin like toxin and a heterologous linker amino acid sequence, linking the A and B chains, wherein the linker sequence contains a cleavage recognition site for a specific protease, wherein the specific protease is an MMP or UPA.

Art Unit: 1645

The teachings of Borgford (WO 97/41233) are set forth above.

Borgford do not teach of specific proteases which are MMP or UPA.

Kappler et al (US Patent Number 5,820,866) teach that the use of linkers for fusing proteins comprising metalloproteases (MMPs) was well known at the time of the instant invention. (See column 10).

Given that 1) Borgford has taught of a protein having an A chain of a ricin-like toxin, a B chain of a ricin like toxin and a heterologous linker comprising a specific protease, and that 2) Kappler et al has taught of the advantages of using a metalloprotease as a linker, it would have been prima facie obvious to have incorporated the metalloprotease as the linker as taught by Kappler in the fused molecule of A chain ricin like toxin and B chain ricin like toxin as taught by Borgford. One would have been motivated to produce such a molecule in view of the success of Kappler using a metalloprotease as a linker, and the success of Borgford using a linker which is already a protease.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory

Art Unit: 1645

double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 13-21, 37-38, 42 and 45 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,333,303. Although the conflicting claims are not identical, they are not patentably distinct from each other because each set of claims encompasses recombinant proteins comprising an A chain of a ricin toxin and a B chain of a ricin toxin linked by a sequence which contains a cleavage recognition site for a protease.

9. Claims 13-21, 37-38, 42 and 45 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 6,531,125. Although the conflicting claims are not identical, they are not patentably distinct from each other because each set of claims encompasses recombinant proteins comprising an A chain of a ricin toxin and a B chain of a ricin toxin linked by a sequence which contains a cleavage recognition site for a protease.

10. Claims 13-21, 37-38, 42 and 45 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,803,358. Although the conflicting claims are not

Art Unit: 1645

identical, they are not patentably distinct from each other because each set of claims encompasses recombinant proteins comprising an A chain of a ricin toxin and a B chain of a ricin toxin linked by a sequence which contains a cleavage recognition site for a protease.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro whose telephone number is (571) 272-0861.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1645

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Mark Navarro  
Primary Examiner  
June 23, 2005